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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,780	10/20/2005	Yafan Huang	22542-010 NATL	1359

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EXAMINER	
MEHTA, ASHWIN D	

ART UNIT	PAPER NUMBER
1638	

MAIL DATE	DELIVERY MODE
12/15/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,780	HUANG ET AL.	
	Examiner	Art Unit	
	Ashwin Mehta	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 7, 10, 13-22, 25-47, and 49-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7,10,13-22,25-47 and 49-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 29, 2008 has been entered.

2. Examination of the instant application has been transferred to Examiner Ashwin Mehta. The art unit, 1638, remains the same.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The objections to claims 6-8 are withdrawn in light of their amendments.

Claim Objections

5. Claim 51, 54, and 56 are objected to because of the following informalities:

In claim 51: the claim is missing the period punctuation mark.

In claims 54 and 56: the recitation, “claims" should be singular.

Appropriate correction is required.

6. Claims 22 and 47 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 22 depends on claim 21, which indicates that SEQ ID NO: 5 is operably linked to a non-translatable mRNA molecule of a gene encoding a protein of interest. Claim 22 limits the non-translatable mRNA molecule to being an antisense nucleic acid, hairpin RNA, or microRNA. However, while these mRNAs may be non-translatable, none of them encode a protein. Claim 22 encompasses limitations that are not encompassed by claim 21, and can be infringed without also infringing claim 21. See MPEP 608.01(n) III.

Claim 47 limits the method of claim 46. The method of claim 46 comprises introducing into a plant cell the vector of claim 10, which contains the isolated nucleic acid molecule of claim 1, which regulates "constitutive tissue specific expression". It is unclear what this recitation means (see the indefinite rejection below). However, if the nucleic acid molecule of claim 1 directs expression of an operably linked nucleotide sequence in a tissue-specific manner, then claim 47 encompasses an embodiment that is not encompassed by claim 46. Claim 47 limits the method of claim 46 by requiring expression to be constitutive, which according to the definition in the paragraph bridging pages 12-13, means expression in all or nearly all tissues of a plant.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 7, 10, 13-20, 31-40, 46, 47, 49, 50, and 54-62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1: the recitation, "constitutive tissue specific" renders the claim and those depending thereon indefinite. The paragraph bridging pages 12-13 of the specification states, "The terms "constitutive promoter" as used herein refer to a promoter which is capable of expressing operably linked DNA sequences in all tissues or nearly all tissues of a plant." Given this definition, it is unclear what kind of specificity is attributed to a "constitutive tissue specific" promoter, given that a constitutive promoter is to be considered one that is active in all or nearly all tissues of a plant. It is noted that dependent claim 62 recites, "said tissue specific transcription is in aerial plant tissue". However, it is unclear how this further limits the recitation, "constitutive tissue specific".

Further, the recitation "tissue specific" also renders the claims indefinite. The recitation does not define the tissue that expression is specific for.

Further in claim 1: the recitation, "wherein said nucleic acid molecule regulates constitutive tissue specific transcription of an operably linked nucleotide sequence of interest" also renders the claim indefinite. It is unclear if the nucleotide sequence of interest is, or is not, part of the product encompassed by claim 1. Dependent claim 10 is directed to an isolated nucleic acid construct comprising the nucleic acid molecule of claim 1, operably linked to a heterologous gene, which suggests that claim 1 does not

encompass the nucleotide sequence of interest. However, dependent claim 7 limits the type of nucleotide sequence of interest mentioned in claim 1, which does suggest that the product of claim 1 encompasses the nucleotide sequence of interest. Note that if the product of claim 1 does not encompass a nucleotide sequence of interest, then claim 7 does not further limit claim 1 in any manner.

In claims 54 and 56: there is insufficient antecedent basis in the claims for the limitation, "The transgenic plant". It is suggested that "The" be replaced with --A--.

In claims 55 and 57: there is insufficient antecedent basis for the limitation, "The seed". It is suggested that "The" be replaced with --A--.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 7, 10, 13-20, 31-40, 46, 47, 49, 50, 54, 55, and 58-62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Independent claim 1 is broadly drawn to any isolated nucleic acid molecule a) consisting of SEQ ID NO: 5 or b) less than 487 base pairs in length comprising the nucleotide sequence of SEQ ID NO: 5, wherein the nucleic acid molecule regulates

constitutive tissue specific transcription of an operably linked nucleotide sequence of interest.

The specification provides the nucleotide sequence of SEQ ID NO: 5 in the sequence listing and in Table 2B on page 59. However, the specification does not provide written descriptive support for an isolated nucleic acid molecule that is "less than 487 base pairs in length comprising the nucleotide sequence of SEQ ID NO: 5". This recitation is NEW MATTER and must be removed from the claims.

9. Claims 1, 7, 10, 13-20, 30-40, 46, 47, 49, 50, 54, 55, and 58-62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Independent claim 1 is broadly drawn to any isolated nucleic acid molecule a) consisting of SEQ ID NO: 5 or b) less than 487 base pairs in length comprising the nucleotide sequence of SEQ ID NO: 5, wherein the nucleic acid molecule regulates constitutive tissue specific transcription of an operably linked nucleotide sequence of interest.

Claim 1 indicates that SEQ ID NO: 5 or an isolated nucleic acid molecule less than 487 base pairs comprising SEQ ID NO: 5 has constitutive tissue specific transcriptional activity. As discussed above, it is not exactly clear what is meant by "constitutive tissue specific", given the definition for "constitutive" in the specification. In the response filed September 29, 2008, Applicants discuss the amendments to claim 1

as if this recitation indicates that SEQ ID NO: 5 is tissue specific. However, the specification does not enable such an embodiment. Page 5 of the specification indicates that SEQ ID NO: 4 is the full length Arabidopsis HRP gene promoter, and SEQ ID NO: 5 is a truncation of that promoter, that the HPR promoter demonstrates expression in aerial tissues, and that the modification of SEQ ID NO: 5 includes root expression (page 5, 1st paragraph under "DETAILED DESCRIPTION OF INVENTION"). The promoter analysis presented in Example 9 on pages 64-65 teaches that the promoter of SEQ ID NO: 4 (in the pHPR-GUS construct) showed activity in aerial tissue of young seedlings but no detectable expression in roots, and that SEQ ID NO: 5 (in the pHPRT-GUS construct) showed expression in roots in addition to the staining of aerial tissues. The specification does not define "aerial", and therefore it is unclear if the additional transcriptional activity in roots means that tissue specificity is actually lost in SEQ ID NO: 5. The Merriam Webster's Collegiate Dictionary (10^{th} Ed., 1996) defines "aerial" as "of, relating to, or occurring in the air or atmosphere", and "existing or growing in the air rather than in the ground or in water." If "aerial" is to mean any plant tissue above the ground, then the added transcriptional activity in roots indicates that tissue specificity is lost in SEQ ID NO: 5. Parts of the plants produced in the promoter analysis discussed in Example 9 are shown in Figure 3. However, only informal and unclear black and white drawings of that figure have been submitted. These informal drawings are unclear and do not allow one to discern where the HPR promoters are, and are not, active. Therefore, given that 1) the specification in Example 9 teaches that SEQ ID NO: 5 has transcriptional activity in both aerial and root tissues, 2) the specification does not define "aerial", and 3) the dictionary definition for "aerial" implies "existing or growing in the

air rather than in the ground", it appears that the promoter of SEQ ID NO: 5 is not tissue specific. The specification does not mention at all any isolated nucleic acid molecule less than 487 base pairs in length comprising SEQ ID NO: 5, or any properties of such a molecule. See *Genentech, Inc. v. Novo Nordisk, A/S*, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention. Given the breadth of the claims, unpredictability of the art, and teachings of the specification that SEQ ID NO: 5 is active in plant tissues that are above the ground, as well as in roots, undue experimentation would be required by one skilled in the art to use the claimed nucleic acid molecule in a tissue specific manner.

If "constitutive tissue specific" does not refer to a promoter that is "tissue specific", then this aspect of the rejection is moot.

Further, in claims 20 and 30: Claim 20 limits the nucleotide sequence of interest operably linked to the nucleic acid molecule of claim 1, to encoding a CaaX prenyl protease. Claim 30 limits the non-translatable mRNA of a gene of a protein of interest, which is operably linked to SEQ ID NO: 5, to encoding CaaX prenyl protease. However, neither the specification nor the prior art teach an isolated nucleotide sequence encoding a CaaX prenyl protease. In the absence of further guidance, undue experimentation would be required by one skilled in the art to isolate a gene encoding said protease. See In re Bell, 26 USPQ2d 1529, 1532 (Fed. Cir. 1993) and In re Deuel, 34 UPSQ2d, 1210 (Fed. Cir. 1995), which teach that the mere existence of a protein does not enable claims drawn to a nucleic acid encoding that protein.

Claim Rejections - 35 USC § 103

10. Claims 1, 7, 10, 13-22, 25-47, and 49-61 remain rejected under 35 U.S.C. 103(a) as obvious over Harper et al. "1" (WO 2002/16655, published February 28, 2002) in light of Harper et al. "2" (GenBank Accession No. AX510060) and Harper et al. "3" (GenBank Accession No. AX507376), for the reasons of record stated in the previous Office action. Applicants traverse in the papers filed September 29, 2008. Applicants' arguments were fully considered but were not persuasive.

Applicants argue that the references do not provide any reason to modify the teachings therein and fail to provide a reasonable expectation of success that truncation of the promoter of Harper would successfully provide the claimed tissue specific constitutive promoter (response, paragraph bridging pages 7-8 and page 8, 1st full paragraph). However, first, as discussed above, it is unclear how "constitutive tissue specific" is to be defined in the context of the claimed invention, given the definition of "constitutive" in the instant specification on page 12. Applicants' use of the term "constitutive" in their arguments is inconsistent with the definition provided in the instant specification. The recitation makes it unclear what properties are possessed by the claimed nucleic acid molecule, as claim 1 is currently written and read in light of the specification.

Applicants argue that Harper discloses SEQ ID NOs: 2071 and 4755, each of which include instant SEQ ID NO: 5, and that SEQ ID NO: 4755 functions as an inducible promoter in response to abiotic stress (response, page 8, 2nd full paragraph). However, the instant claims do not preclude the promoter from being inducible.

Applicants' argument is confusing, given that the instant specification admits that the HPR promoter is inducible by environmental stress (pages 2, 5, 64, for example).

Applicants also argue that there is nothing in Harper to suggest that anything less than the 487 base pair sequence of SEQ ID NO: 4755 is desirable. Applicants argue that the Examiner's citation of Singh in the previous Office action provides only one example of truncating a promoter in the prior art, and that Singh does not teach or suggest truncation of other promoters would result in identification of core promoter sequences, no less to create a tissue specific constitutive promoter (response, page 8, 2nd full paragraph and the paragraph bridging pages 8-9). However, Harper et al. do discuss that promoters contain several domains necessary for full activity, that they contain a "core promoter region" necessary for minimal transcriptional activity, and discuss how to define such a region (page 35). Further, Applicants' own specification discusses several prior art publications wherein deletion analyses were conducted on a cucumber HPR promoter, which identified regions necessary for tissue specificity (page 8, 1st full paragraph). This indicates that promoter deletion analysis was routinely conducted in the prior art, and that Applicants were even aware of it being conducted on another plant HPR promoter. Given the teachings of the prior art, it would have been obvious to also conduct promoter deletion analysis on the HPR promoter of SEQ ID NO: 4755 of Harper et al.

Applicants continue, arguing that Harper fails to provide a reasonable expectation of success that truncation of SEQ ID NO: 4755 would result in tissue specific transcription, as required by the claims and supposedly demonstrated in the instant application. Applicants direct attention to instant Figures 3B and C as demonstrating that

promoter activity of SEQ ID NO: 5 is primarily restricted to aerial tissues, demonstrating tissue specific transcription (response, page 9, 1st full paragraph). However, the specification also shows that SEQ ID NO: 4 is aerial tissue specific. Further, the specification teaches that SEQ ID NO: 5 also directs expression in roots. Therefore, as discussed above, if "aerial" is to mean any plant tissue above the ground, than this property is actually retained in the truncated promoter. However, since SEQ ID NO: 5 also directs expression in roots, it may have lost tissue specificity, and have transcriptional activity in all, or nearly all, plant tissues, which meets the definition of "constitutive" in the specification. Given the indefiniteness of the recitation, "constitutive tissue specific", it is unclear what properties are to be possessed by the claimed nucleic acid molecule. Given that promoter deletion analysis was routine in the prior art to determine regions necessary for minimal activity as well as domains necessary for other properties including tissue specificity, as discussed by Harper et al. and as admitted in Applicants' specification even for another plant HPR promoter, it would have been obvious to conduct such an analysis on the promoter of SEQ ID NO: 4755 of Harper et al., to arrive at truncated promoters, including SEQ ID NO: 5, with a reasonable expectation of success.

Contact Information

Any inquiry concerning this or earlier communications from the Examiner should be directed to Ashwin Mehta, whose telephone number is 571-272-0803. The Examiner can normally be reached from 8:00 A.M to 5:30 P.M. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Anne Marie Grunberg, can be reached at 571-272-0975. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic

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December 15, 2008

/Ashwin Mehta/
Primary Examiner, Art Unit 1638